

*Annual Review of Public Health*

# Health Risks and Benefits of Fluoride Exposure During Pregnancy and Infancy

Christine Till,<sup>1</sup> Philippe Grandjean,<sup>2,3</sup>  
E. Angeles Martinez-Mier,<sup>4</sup> Howard Hu,<sup>5</sup>  
and Bruce Lanphear<sup>6</sup>

<sup>1</sup>Faculty of Health, York University, Toronto, Ontario, Canada; email: ctill@yorku.ca

<sup>2</sup>Department of Biomedical and Pharmaceutical Sciences, University of Rhode Island, Kingston, Rhode Island, USA

<sup>3</sup>Department of Public Health, University of Southern Denmark, Odense, Denmark

<sup>4</sup>Department of Dental Public Health and Dental Informatics, School of Dentistry, Indiana University, Indianapolis, Indiana, USA

<sup>5</sup>Keck School of Medicine, University of Southern California, Los Angeles, California, USA

<sup>6</sup>Faculty of Health Sciences, Simon Fraser University, Vancouver, British Columbia, Canada

ANNUAL  
REVIEWS **CONNECT**

[www.annualreviews.org](http://www.annualreviews.org)

- Download figures
- Navigate cited references
- Keyword search
- Explore related articles
- Share via email or social media

Annu. Rev. Public Health 2025. 46:253–74

The *Annual Review of Public Health* is online at [publhealth.annualreviews.org](http://publhealth.annualreviews.org)

<https://doi.org/10.1146/annurev-publhealth-060722-023526>

Copyright © 2025 by the author(s). This work is licensed under a Creative Commons Attribution 4.0 International License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. See credit lines of images or other third-party material in this article for license information.



## Keywords

fluoride, risk–benefit, systemic exposure, neurotoxicity, pregnancy, fluoridation

## Abstract

Health authorities have promoted community water fluoridation (CWF) to prevent dental caries for more than 75 years. However, growing evidence has raised questions about the safety of this public health intervention, particularly for young children who are at risk of excess fluoride intake. Divergent opinions about the risk–benefit ratio of CWF have ignited a global debate. The efficacy of topical fluoride in preventing dental caries is strong, whereas contemporary evidence for systemic administration of fluoride is weaker. Inequalities in access to dental care and topical fluorides introduce an additional layer of complexity. This review discusses evidence showing that fluoride ingestion is not essential for caries prevention, offers little benefit to the fetus and young infant, and can cause dental fluorosis and cognitive deficits. In an environment where fluoride is available from multiple sources, community-based administration of systemic fluoride may pose an unfavorable risk–benefit ratio for pregnant women and young children.

## 1. INTRODUCTION

Community water fluoridation (CWF) was introduced in the 1940s to combat the rise in dental caries (i.e., tooth decay) following an increase in sugar consumption (84). Studies conducted from the 1940s through the 1970s showed that fluoridated drinking water reduced dental caries by about two-thirds in children (20). About 420 million people worldwide have access to naturally fluoridated water supplies (50 million) or artificially fluoridated drinking water (370 million) (109). The United States, Brazil, Malaysia, Australia, and Canada have the largest populations of people supplied with artificially fluoridated water (**Supplemental Figure 1**), while other countries have adopted community-level fluoridation of salt or milk (109). Despite advances in caries prevention and management over the past 75 years, untreated caries affect 43% of the world population (145) (see the sidebar titled Community Water Fluoridation).

Fluoride is considered safe by health officials when consumed at recommended levels. But a growing body of evidence has linked systemic fluoride exposure with detrimental effects on bone strength (71, 92), thyroid function (74), and brain function (57, 105, 129). Excessive fluoride exposure is particularly hazardous for young children due to the vulnerability of the developing brain (87).

This review focuses on the scientific evidence relevant to populations living in areas with fluoride exposures below the World Health Organization (WHO) limit of 1.5 mg/L in drinking water (145). We aim to characterize the effectiveness of fluoride with a discussion of how and when fluoride works to prevent dental caries. We then assess the adverse effects of fluoride exposure on enamel fluorosis, pregnancy outcomes, thyroid function, and child neurodevelopment. Next, we discuss current guidelines for fluoride use in pregnancy and early childhood issued by scientific and regulatory institutions. Finally, we explore the challenges of bridging the gap between public health policies and scientific evidence on the health effects of fluoride ingestion.

## 2. SOURCES OF FLUORIDE EXPOSURE

The main sources of fluoride intake are fluoridated water or fluoridated salt, as well as some foods, drinks, and oral fluoride supplements. For adults, drinking fluoridated water and consuming foods and beverages made with fluoridated water account for 70–75% of total fluoride intake (134). Average fluoride concentrations in bottled water are 0.11 mg/L; more than 90% of bottled water contains fluoride concentrations below 0.3 mg/L (11).

Powdered infant formula mixed with fluoridated water is a significant source of fluoride (91). In the United States, 70–75% of caregivers reportedly mix powdered infant formula with tap water (21). If fluoridated tap water is used, the fluoride concentration in infant formula ranges from 0.76 to 0.83 mg/L compared with 0.05 to 0.13 mg/L if deionized water is used (67). The concentration of fluoride also depends on the type of formula (14). Soy-based formulas contain higher fluoride levels (2.52 mg/L) compared to milk-based formulas (0.22–0.31 mg/L) prepared with deionized water (101). In contrast, breast milk has extremely low fluoride levels (<0.02 µg/L) (40, 42, 153).

### COMMUNITY WATER FLUORIDATION

Community water fluoridation is endorsed by many national and international health organizations as an effective way to reduce dental caries. The recommended fluoride concentration in drinking water typically ranges between 0.7 and 1.1 mg/L. Some countries, including over 97% of Europe, have opted for targeted strategies, including fluoride-containing toothpaste and adding fluoride to milk or salt.

Young children often swallow toothpaste (126, 130). Ingestion of toothpaste by young children is estimated to account for up to 80% of total dietary fluoride intake depending on the age of the child, frequency of brushing, and amount and type of toothpaste used (113). Nearly 40% of US children aged 3–6 years used more than the pea-size amount of toothpaste recommended by health authorities (130); 18% used a full load of toothpaste.

Fluoride levels are high in some foods, including seafood containing edible bones (e.g., sardines), fruits and vegetables with fluoride-containing pesticides, gelatins, mechanically deboned meat (e.g., chicken nuggets), and foods grown in fluoride-contaminated soil (17, 116). Tea plants are capable of hyperaccumulating fluoride from soil, with fluoride concentrations in brewed tea ranging from 0.31 to 8.9 mg/L (25, 85). In the Republic of Ireland, where consumption of black tea per capita is among the highest in the world, the total intake of fluoride from tea can exceed the upper safe limit for adults and children (143). Finally, fluoride can be released by some pharmaceuticals, including fluoridated anesthetics.

### 3. FLUORIDE ABSORPTION, DISTRIBUTION, AND EXCRETION

Ingested fluoride is rapidly absorbed in the stomach and intestines, with plasma fluoride concentrations reaching a peak within 20–60 min. Infants and young children retain 80–90% of absorbed fluoride (41) compared with 50% in healthy adults (16). About 99% of the body's fluoride is strongly bound to mineralized tissues (mainly bone); about 1% is found in soft tissues, including calcified parts of the pineal gland (93). Fluoride is mobilized from continuous skeleton remodeling. In contrast, fluoride in teeth is mobilized only during remineralization and demineralization cycles with dental caries formation. Fluoride that is absorbed or released from calcified tissues enters the systemic circulation and is eliminated by the kidneys (16).

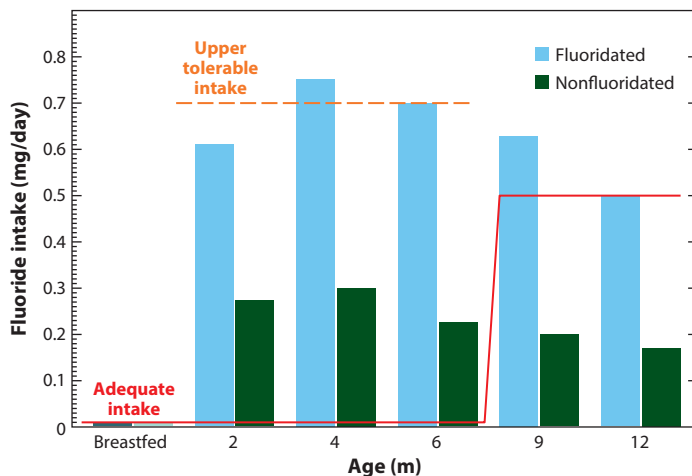
Fluoride absorption is influenced by pharmacokinetic factors, including blood pH, dietary intake of calcium and other cations, and pregnancy-related renal changes (16, 19). In pregnancy, urinary fluoride concentrations have been found to increase toward the end of gestation (95, 132). Reasons for this trend are unclear but may reflect uptake of fluoride into fetal bone or increased mobilization of fluoride from maternal bone (110). In infants, fluoride absorption may be reduced by coagulation of milk in the stomach due to acidity and calcium fluoride formation, meaning that less fluoride is absorbed from milk-based relative to soy-based formulas (23).

Once fluoride reaches the plasma, it is rapidly bound to the skeleton or excreted through the kidneys, with only a small amount of unabsorbed fluoride excreted in the feces. Urine is the most commonly used biomarker for estimating short-term fluoride exposures, whereas fasting samples may be more suitable for measuring chronic fluoride intake (119). Historically, the concentration of fluoride measured in biological samples, such as urine or blood, has resembled the concentration found in drinking water (104, 109); if the water fluoride concentration is 1.0 mg/L, then urinary and plasma fluoride concentrations are approximately 1.0 mg/L and 1.0  $\mu\text{mol/L}$ , respectively (86).

Fluoride readily crosses the placenta (110, 136), penetrates the blood–brain barrier (47, 49, 133), and accumulates in the cerebellum, motor cortex, and hippocampus (34, 47). The rate of diffusion depends on the fluoride concentration; lower concentrations passively diffuse across the placenta, but transport is attenuated at higher concentrations (63). In a study of 22 women living in an area where drinking water fluoride concentration was  $<0.5$  mg/L, maternal and neonatal fluoride serum concentrations were similar at delivery (121).

### 4. ADEQUATE INTAKE LEVELS FOR FLUORIDE

The adequate intake (AI) level for fluoride in the first 6 months of life has been set at 0.01 mg/day, equivalent to 1 tablespoon of optimally fluoridated water. Among formula-fed infants younger



**Figure 1**

Dietary fluoride intake of infants aged 2 to 12 months by varying concentrations of fluoride in water used to reconstitute formula. The red solid line shows adequate intake (AI) levels by age; the orange dashed line shows the upper tolerable limit (78). Green bars show the total fluoride ingested from formula reconstituted with low-fluoride water (<0.3 mg/L) across different types of infant formulas. Light blue bars show the total fluoride ingested from formula reconstituted with water that is optimally fluoridated at 0.7 mg/L. Data for infants aged 2 to 12 months extrapolated from Reference 67. Using reference weights of each age group, the AI level is 0.5 mg/day for infants aged 7 to 12 months, 0.7 mg/day for children aged 1 to 3 years, and 1.0 mg/day for children aged 4 to 8 years (78).

than 6 months, daily fluoride intake is about 0.61–0.75 mg/day (about 60–70 times the AI) if fluoridated water is used versus 0.23–0.30 mg/day if low-fluoride water is used to reconstitute formula (**Figure 1**) (67, 122). The maximum safe daily intake level (i.e., upper tolerable level) for infants younger than 6 months is 0.7 mg/day, but intake can exceed this limit in some formula-fed infants (91). For all other life stages, 0.05 mg per kg of bodyweight is the accepted level for daily intake of fluoride to maximize caries prevention while minimizing risk of dental fluorosis (39, 78, 103).

Defining an optimal fluoride intake has been controversial (see the sidebar titled Fluoride Is Not an Essential Element). Fluoride prevents caries when it is in contact with dental surfaces in the oral environment, known as a topical effect (15). Even when fluoride intake is considered optimal, studies have found that a sizable fraction of the population will develop caries (142). Formation of dental caries is influenced by diverse biological factors, such as biofilm composition, metabolism, saliva, diet, and potentially genetics. Use of topical fluorides (e.g., toothpaste) may also explain why a person’s fluoride intake is not a strong predictor for caries. Given the lack of contemporary evidence linking the AI level with caries prevention and reduced risk of dental fluorosis, some experts have concluded that “recommending an ‘optimal’ fluoride intake is problematic” (142, p. 6).

## 5. BENEFITS OF FLUORIDE FOR THE PREGNANT WOMAN, FETUS, AND INFANT

Sugar intake is the most important risk factor for dental caries (100, 145). Sugar consumption, which far exceeds WHO recommendations in high- and middle-income countries, is steadily rising in lower-income countries (145). The widespread availability of free sugars in contemporary diets has made sugar consumption a global public health crisis.

## FLUORIDE IS NOT AN ESSENTIAL ELEMENT

Some regulatory or advisory agencies, including the US Institute of Medicine (78), the National Health and Medical Research Council in Australia (103), and the European Food and Safety Authority (39), have established dietary reference values for fluoride, which are reported as adequate intake (AI) values from all sources. In contrast, the WHO, the Scientific Committee for Food, and the Netherlands Food and Nutrition Council have no AI level for fluoride because it is not considered to be essential for human growth and development.

Dental caries result when free sugars contained in food or drink are converted by bacteria into acids that demineralize the enamel. The presence of proteins and ions—including fluoride—in the oral environment neutralizes these acids and promotes remineralization, thus preventing the formation of caries. Fluoride exerts anticariogenic action via three mechanisms: slowing demineralization, promoting remineralization of enamel by enhancing the precipitation of hydroxyfluorapatite, and inhibiting bacterial metabolism and acid production (44).

### 5.1. When Does Fluoride Benefit Teeth?

In the 1940s, fluoride's incorporation into the developing enamel (i.e., pre-eruptively) was thought to make teeth less soluble and more resistant to dental caries (33). However, laboratory and epidemiological studies conducted over the past 50 years have shown that fluoride's beneficial effect is predominantly topical, after tooth eruption (45, 46). Results of a randomized, double-blind trial (88) and a Cochrane review (128) showed that fluoride supplements taken by pregnant women do not benefit their offspring (see the sidebar titled Guidelines for Fluoride Use in Infancy and Pregnancy).

A reanalysis of data from the Tiel–Culemborg study (62), along with more recent cohort studies (123, 124), indicated that pre-eruptive fluoride exposure may be beneficial for certain surfaces, particularly pits and fissures of permanent molars, as these areas are highly susceptible to caries and difficult for topical fluorides to reach. However, the limited data available make it challenging to draw definitive conclusions about the relative contribution of systemic fluoride treatment before

## GUIDELINES FOR FLUORIDE USE IN INFANCY AND PREGNANCY

**Pregnant women:** The American Dental Association recommends that pregnant women continue to brush twice a day for 2 min with toothpaste that has fluoride. Prenatal fluoride supplements are not recommended.

**Infants 0–6 months:** The American Academy of Pediatrics (AAP) (28) recommends breastfeeding for the first year of a baby's life. The AAP does not recommend fluoride supplements. If breastfeeding is not possible, fluoridated tap water can be used to reconstitute formula, but the AAP recognizes a small risk for fluorosis in the permanent dentition. To lessen the chance for fluorosis, caregivers can use low-fluoride water to mix infant formula or ready-to-feed formula. Examples of low-fluoride water include bottled water labeled as low in fluoride or deionized, purified, demineralized, or distilled water.

**Children 7 months through 3 years:** The AAP recommends using no more than a smear of fluoride toothpaste the size of a grain of rice, twice a day, under the supervision of an adult. After tooth emergence, the AAP advises that optimally fluoridated water be used to reconstitute formula.

**Children 3–6 years:** The AAP recommends using no more than a pea-size amount of fluoride toothpaste, twice a day, under the supervision of an adult who can encourage spitting out excess toothpaste.

teeth erupt. A consensus has now emerged that the primary protective effects of fluoride are topical (12, 128).

## 5.2. Topical Versus Systemic Fluoride Sources

Topical fluoride exposure, such as brushing with fluoride toothpaste (13, 45), delivers fluoride to the interface between the tooth surface (enamel) and the oral fluids. Daily use of fluoride toothpaste with  $\geq 1,000$  ppm is shown to be effective for caries prevention in children (139). Hydroxyapatite-based and arginine (i.e., fluoride-free) toothpastes are being investigated as an alternative to fluoride toothpaste (3, 108, 112).

Systemic fluoride, such as fluoridated drinking water, can also have an anticaries effect through contact with enamel when it enters the oral cavity and when absorbed fluoride is recirculated in saliva (15, 44). Thus, CWF is a systemic method for fluoride delivery, but its mechanism of action to control caries is through its topical contact with teeth.

## 5.3. Benefits of Community Water Fluoridation

CWF has been associated with a 25% relative reduction in dental caries in children and adults (22, 61). However, a 2015 Cochrane review indicated that the evidence supporting CWF was of low-quality and that 71% of the studies were conducted prior to 1975, before toothpaste and other fluoride treatments became widely available (76). A 2024 Cochrane review of 21 studies conducted after 1975 indicated a much smaller benefit of CWF compared with pre-1975 studies. The authors estimated a reduction in the number of decayed, missing, and filled primary teeth of not more than 4% or possibly no benefit given the uncertainty of the estimate (77). These findings suggest that fluoride in water may reduce tooth decay only by about one-quarter of a tooth. The authors also concluded that there is limited contemporary evidence to determine whether CWF reduces social disparities in dental caries (77). The Cochrane findings are consistent with a recent study of 6.4 million people in the United Kingdom showing that the number of decayed, missing, and filled teeth was only 2% lower among people living in fluoridated versus nonfluoridated areas (98). Taken together, contemporary evidence indicates that the caries-reduction benefits of CWF when combined with regular topical fluoride use are smaller today (77, 98) (**Figure 2**; see also the sidebar titled Caries Prevalence).

## 6. RISKS FOR THE FETUS, YOUNG CHILD, AND PREGNANT WOMAN

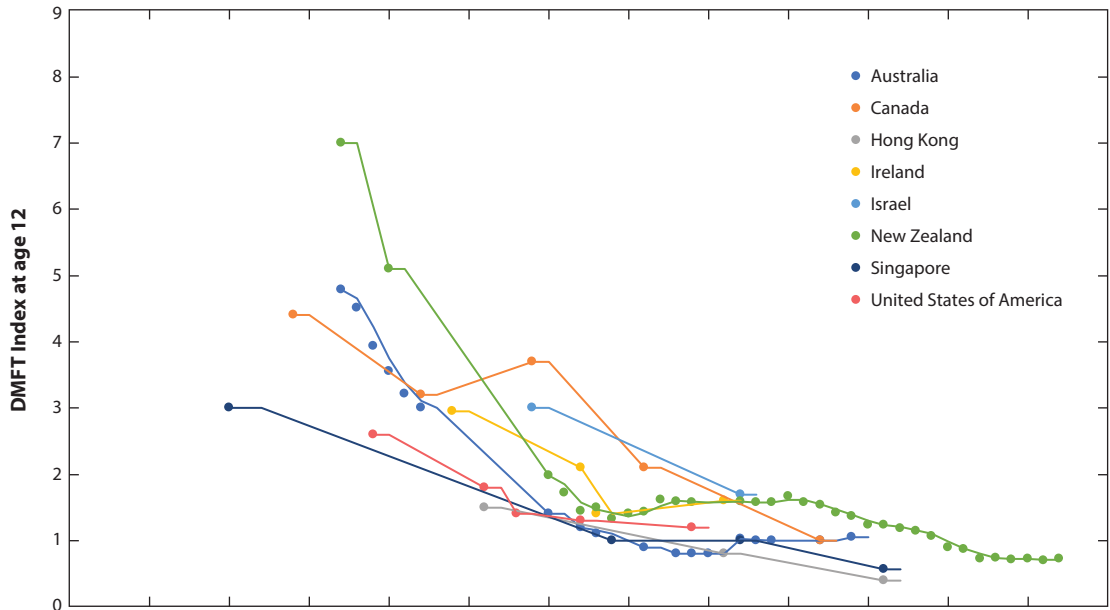
### 6.1. Risks of Dental Fluorosis

Dental fluorosis is a developmental defect of tooth enamel due to excessive fluoride intake during the pre-eruptive period (35, 147). High fluoride exposure before tooth eruption disrupts the formation of hydroxyapatite crystals (main component of the enamel mineral matrix) causing

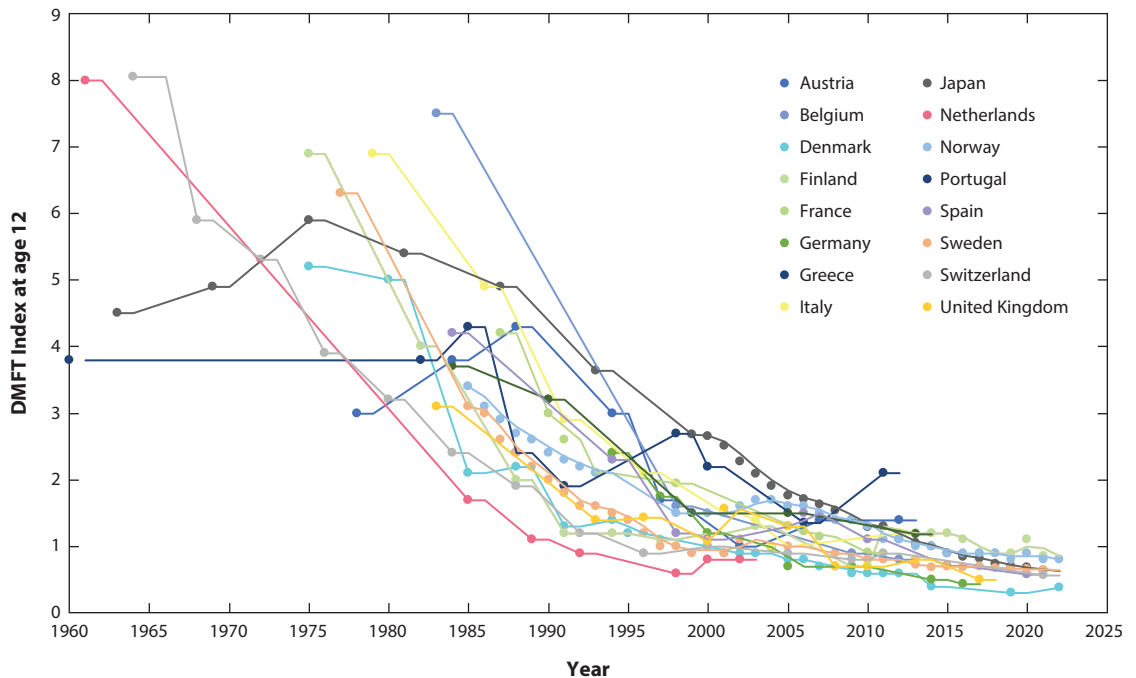
## CARIES PREVALENCE

WHO data from the 1970s onward show almost uniform rates of decline in caries prevalence in several developed countries, regardless of fluoridation of water supplies (**Figure 1**). This decline has been attributed to widespread use of fluoride toothpastes, an increase in access to dental care, and other factors, such as nutrition. While caries in deciduous teeth have been declining among upper-middle- and high-income countries, dental caries rates are on the rise in lower-income countries, likely due to increased sugar consumption.

**a** Dental caries trends in fluoridated countries



**b** Dental caries trends in nonfluoridated countries



**Figure 2**

Dental caries trends as indicated by the Decayed, Missing, or Filled Permanent Teeth (DMFT) Index for 12-year-olds in (a) eight fluoridated countries (Australia, Canada, Hong Kong, Ireland, Israel, New Zealand, Singapore, United States) and (b) sixteen nonfluoridated countries (Austria, Belgium, Denmark, Finland, France, Germany, Greece, Italy, Japan, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom). Figure based on Country/Area Profile Program data accessed from the World Health Organization Collaborating Centre for Education, Training, and Research in Oral Health, Malmö University, Sweden (111).

hypomineralization of the enamel subsurface. As a result, the tooth enamel is discolored: Mild fluorosis appears as thin white lines, moderate fluorosis coalesces into larger white areas, and severe fluorosis covers the entire surface, with or without the presence of brown discoloration and pitting. The severity of dental fluorosis relates to the dose, frequency, and timing of fluoride exposure as well as individual susceptibility factors (13). Most dental fluorosis in the United States is very mild to mild (**Supplemental Figure 2**) (36).

The window of susceptibility for dental fluorosis in permanent central incisors, the most aesthetically relevant teeth, is from birth through age 4, but particularly during the first 2 years of life (43). However, overexposure to fluoride during the first 8 years of life can result in fluorosis for the entire permanent dentition (72). Drinking water with fluoride concentrations higher than 1 mg/L contributes to dental fluorosis (90), but dental fluorosis is also prevalent among populations living in optimally fluoridated areas (36, 73). Infants fed formula reconstituted with optimally fluoridated water (89, 90) and young children who swallow fluoride toothpaste have increased risk of developing dental fluorosis (89, 113). In 2015, a Cochrane review estimated that 12% of people would have dental fluorosis of aesthetic concern (i.e., defined as “mild” or worse on Dean’s index) with a water fluoride concentration of 0.7 mg/L; 40% would have any level of fluorosis (76).

The prevalence and severity of dental fluorosis has increased worldwide over the past three decades (10, 102, 106, 146). According to the Oral Health of United States Children survey, 41% of American youth had dental fluorosis that was very mild or greater in 1999–2004, nearly double the prevalence reported in 1987 (135). Likewise, 61% of American youth evaluated as part of the National Health and Nutrition Examination Survey (NHANES) had dental fluorosis that was very mild or greater in 2011–2012 compared with 30% a decade prior (10, 102, 146); the prevalence was even higher (69%) in the NHANES 2015–2016 survey.

The striking increase in dental fluorosis is likely due to the cumulative ingestion of fluoride from various sources in childhood, including appealing candy-flavored toothpaste, and increased exposure to fluoride from ready-to-drink (bottled) tea or iced tea, processed foods, infant formula, mechanically deboned meats, and fluoride pesticide residues on foods. Changes in the indices and technologies used to measure dental fluorosis must also be considered when assessing trends in fluorosis prevalence (38).

Fluid consumption patterns, dental hygiene practices, and socioeconomic characteristics have been investigated as factors that increase risk of dental fluorosis (96). Data from the NHANES 1999–2002 survey showed a higher prevalence of very mild to severe dental fluorosis among non-Hispanic Blacks (26%) compared with non-Hispanic White participants (21%), likely reflecting differences in breastfeeding and water consumption habits in early life (4, 70). Black children and children from low socioeconomic status (SES) have been reported to have higher consumption of drinking water and lower consumption of milk compared with White children or children from affluent backgrounds (125). Significant racial differences have also been observed in fluoride use and dental care: Black children have been reported to use fewer fluoride supplements but more toothpaste and to have higher urine fluoride levels than White children (96). Research into how dietary and nondietary factors as well as sociodemographic characteristics give rise to increased prevalence of dental fluorosis is needed (86).

## 6.2. Risk of Adverse Birth Outcomes

Studies examining the impact of fluoride exposure at levels below 1.5 mg/L on pregnancy outcomes have shown mixed results. One United States–based study reported a significant negative association between gestational fluoride exposure and birth weight (5), whereas a Swedish study reported a positive association (82). Another prospective study conducted in Mexico City (111)



found both increases and decreases in birth weight depending on whether urinary fluoride was measured during early or late pregnancy. A Canadian study found no association with birth weight (52). Studies have not linked gestational exposure to fluoride or CWF with prematurity (52, 82, 151). Finally, higher fluoride levels have been associated with increased risk of being born large for gestational age (51, 82).

Overall, no definitive evidence links fluoride exposure with adverse birth outcomes. However, the current evidence base is limited. The inconsistent results may reflect the wide variation in exposure levels, differences in how exposures were assessed (e.g., water versus urine fluoride levels), and how confounders were controlled. Differences in pregnancy health complications across the cohorts, including gestational diabetes, preeclampsia, or hypothyroidism, may also contribute.

### 6.3. Risk of Thyroid Dysfunction

Fluoride exposure may negatively affect thyroid function in children and adults (74). While the use of fluoride as a thyroid suppressant dates back to the 1930s (32), few studies have examined thyroid functioning in people, particularly pregnant women, living in areas with optimally fluoridated water. Thyroid hormone insufficiency in pregnancy is of particular concern because the developing fetus relies exclusively on maternal thyroid hormone during the first 10–12 weeks of gestation (99).

One Canadian study involving 1,105 pregnant women found that a 0.5 mg/L increase in drinking water fluoride concentration was associated with 1.65 greater odds of having primary hypothyroidism (65); the odds increased to 3.88 among the women with normal levels of anti-thyroid peroxidase antibodies who were living at the same residence for at least one year (66). In this cohort, boys born to women with hypothyroidism had lower IQ scores than children whose mothers had normal thyroid function, suggesting that thyroid disruption may be a mechanism underlying developmental neurotoxicity of fluoride. Moreover, the combination of low iodine, an essential nutrient for thyroid hormone synthesis, and high fluoride exposure in pregnancy was associated with lower IQ scores in boys (54).

Fluoride may disrupt thyroid hormones. A positive association between urinary fluoride levels and thyroid-stimulating hormone (TSH) levels was found among pregnant women carrying baby girls (64). Among the total sample, however, urinary fluoride levels were not associated with maternal free T4 or TSH levels; null findings with fluoride biomarkers were also found in a Swedish pregnancy cohort (82), though this study did not report whether fetal sex modified the associations. The evidence examining the association between exposure to fluoride and disruption to thyroid function is limited for pregnant women living in optimally fluoridated areas. More studies examining thyroid disease risk with measures of iodine status and chronic fluoride exposure are needed given that thyroid disorders tend to develop over time and can be exacerbated by low or excess iodine.

### 6.4. Risks of Adverse Neurodevelopmental Outcomes

The National Toxicology Program (NTP), a federal program in the United States established to study the health effects of chemicals, conducted a comprehensive systematic review (105) and series of meta-analyses evaluating the developmental neurotoxicity of fluoride (129). Unlike other reviews on this topic, the NTP report underwent extensive review by independent scientific committees.

**6.4.1. IQ outcomes.** Among 59 studies reviewed by the NTP, 52 (88%) reported a link between early-life exposure to fluoride and diminished intellectual abilities in children (129). On average, IQ scores were seven points lower among children living in areas with high versus low fluoride exposure levels. When considering only the highest quality studies ( $n = 12$ ), the

association remained significant but was attenuated to a 3-point-lower IQ score among more highly exposed groups. The association between higher fluoride exposure and lower IQ in children remained consistent across sex, age group, study location, exposure metric (urine versus water fluoride), and group- versus individual-level exposure data, adding further support to the NTP's conclusion of an inverse association between early-life fluoride exposure and children's IQ. The findings of the NTP meta-analyses confirmed the results of several previously published meta-analyses on this topic (26, 37, 56, 97, 138) and extended them by including more recently published studies with individual-level exposure measures.

The NTP conducted a series of dose-response meta-analyses, including five studies measuring urinary fluoride (four rated as having low risk of bias) and seven studies measuring drinking water fluoride (three rated as having low risk of bias) at exposure levels <1.5 mg/L. Among the low-risk-of-bias studies, a 1 mg/L increase in urinary fluoride was associated with a decrement of 1.2 IQ points. Among the higher-quality studies with water fluoride levels <1.5 mg/L, the association was also negative, but no longer significant. It is notable that the NTP meta-analyses relied on 4,179 observations (from four studies) with urinary fluoride concentration compared with only 879 observations (from three studies) with water fluoride concentration. Fluoridated water is a major source of exposure, but relying on drinking water alone may underestimate an individual's total fluoride intake because it does not account for variability in volume of water ingested and other non-water fluoride sources. Urinary fluoride, on the other hand, captures all sources of fluoride intake.

Water fluoridation has been practiced for over 75 years, but prospective cohort studies examining whether fluoride poses a risk to the developing brain were not conducted until this past decade. Seven studies from five countries (Canada, Mexico, Spain, Denmark, and Sweden) have examined the effect of gestational fluoride exposure on children's cognitive abilities; four were conducted in areas with optimal salt (18, 53) or water fluoridation (59, 75), one was conducted in an area with endemic fluorosis (137), and two were conducted in areas where fluoride is not added to drinking water but may vary naturally (58, 83). Six of the seven studies included an individual-level urinary fluoride measure, and one estimated fluoride intake from food and beverages. Considering only the prospective, low-risk-of-bias birth cohort studies conducted in optimally fluoridated areas, three of the four studies (18, 53, 59) found a significant inverse association between higher levels of gestational exposure to fluoride and lower child IQ; the Spanish study (75), which did not find an inverse association, measured children's cognitive ability rather than IQ.

Pooling individual observations of 1,599 mother-child pairs from three high-quality prospective cohort studies, the joint benchmark concentration (BMC) for maternal urinary fluoride was 0.45 mg/L, with a BMC lower confidence limit of 0.28 mg/L (58). This BMC is much lower than the WHO's recommendation of 1.5 mg/L as the permissible upper limit for fluoride in drinking water and underscores a critical need for establishing a margin of safety for populations susceptible to developmental neurotoxicity. Precautionary concerns regarding neurodevelopmental effects of fluoride in drinking water were also raised by a risk assessment group commissioned by Health Canada to systematically review current evidence on the human health effects of fluoride (127).

**6.4.2. Susceptible populations.** Bottle-fed infants show heightened susceptibility to fluoride neurotoxicity due to greater exposure by body weight (91). Among formula-fed infants, fluoride intake can be almost 70 times greater compared with an exclusively breastfed infant (40, 134, 153). In one study, infants who were fed formula showed a loss of 4.4 IQ points for each 0.5 mg/L increase in water fluoride concentration; this association remained even after controlling for gestational exposure to fluoride (131). Furthermore, studies have identified effect modifiers that may increase susceptibility to fluoride neurotoxicity. These include iodine deficiency in

pregnancy (54), biological sex (60), and genetic polymorphisms in dopamine receptor D2 or catechol-*O*-methyltransferase (30, 150).

**6.4.3. Behavioral outcomes.** Epidemiological studies conducted in areas with water fluoride concentrations below 1.5 mg/L have reported associations between fluoride exposure and behavioral problems in children. Several high-quality studies have found an association between gestational or contemporaneous fluoride and attention-deficit/hyperactivity disorder (9, 83, 117, 140). A cross-sectional study reported associations between urinary fluoride concentrations (140) and psychosomatic problems and internalizing symptoms in boys. Associations between maternal urinary fluoride and higher risk of internalizing symptoms were also reported in a US pregnancy cohort (94). These studies are concerning, but the body of evidence is limited (48).

**6.4.4. Mechanisms of fluoride neurotoxicity.** Mechanistic studies have found that fluoride can disturb synaptic plasticity (2), alter neurotransmitter levels and intercellular signaling molecules (24), induce mitochondrial dysfunction (1, 141), enhance oxidative stress (47, 79), inhibit metallo-proteins (8, 79), and trigger ferroptosis in the hippocampus of mice (152), a form of programmed cell death involved in the pathophysiology of neurological disorders. Moreover, studies examining aborted fetuses from fluoride endemic areas in China have found alterations in neurotransmitters (149), decreases in neural receptors (149), and stunted neuronal development (69). While data are insufficient to identify a clear mechanism underlying fluoride neurotoxicity, the combination of epidemiological and experimental studies support the conclusion that chronic exposure to fluoride can have deleterious effects on a wide range of cellular, biochemical, and endocrine processes (2, 8, 79).

**6.4.5. Synthesis of current literature.** A large body of evidence supports a consistent, inverse association between fluoride exposure during early brain development and children's IQ (129). Significant and inverse associations have been reported between maternal urinary fluoride levels—a biomarker that captures all sources of exposure—and lower child IQ scores among populations living in optimally fluoridated areas. Adding to this evidence, the BMC level derived from three high-quality prospective cohort studies indicates that current exposure levels among pregnant women are too high to protect against neurocognitive effects in children. Based on the current epidemiological literature, thyroid disruption has been proposed as a possible mechanism of fluoride neurotoxicity, but more research is needed.

## 7. DISCUSSION

CWF is facing growing scrutiny. When it was first introduced, fluoride toothpaste was not available, and it was assumed that fluoride needed to be ingested before teeth erupt to prevent dental caries (33). It is now established that the beneficial effect of fluoride is topical, occurring almost exclusively after teeth erupt (44–46). Fluoride's topical cariostatic mechanism brings into question the necessity of an entire population ingesting fluoride to prevent dental caries when contemporary evidence shows much smaller preventive benefits compared with when it was first introduced (77). Some health authorities assert that consuming fluoride during pregnancy and infancy at levels consistent with national fluoridation standards poses no harm (22). Currently, the only accepted risk associated with CWF is dental fluorosis, but its impact is thought to be minimal (i.e., of aesthetic concern) (78). However, recent evidence shows that fluoride is not just affecting teeth, but also impacting brain development (129) and potentially thyroid function (65).

### 7.1. Need for a Margin of Safety

A key focus of the ongoing scientific debate on fluoride safety centers around whether fluoride in drinking water at levels below 1.5 mg/L is safe. A growing and robust body of evidence

reviewed by the NTP (129) indicates a link between fluoride intake and reduced child IQ, which is a more consequential outcome than dental fluorosis. At high intake levels, it is not disputed that fluoride poses a hazard to human health. However, evidence has now linked urinary fluoride concentrations below 1.5 mg/L to reduced child IQ. This finding has raised concern because urinary fluoride levels for pregnant women and children can exceed this level depending on the amount of fluoridated water ingested and exposure to other fluoride sources. Urinary fluoride levels represent an aggregate of total fluoride intake, with fluoridated water a significant contributor (118, 132, 134). These findings underscore the need for current guidelines to have a margin of safety between a hazard level and the community's exposure level. Thus, if 4 mg/L is an accepted hazard level for fluoride in drinking water, a default 10× margin of safety would require a concentration of 0.4 mg/L to protect the developing child.

Sources of fluoride intake must be monitored. The prevalence and severity of dental fluorosis has steadily increased (10, 38, 102, 106, 146), suggesting that excess fluoride exposure during tooth enamel formation has been occurring over the past few decades. With over two-thirds of children and adolescents having dental fluorosis (100)—an outcome that AI levels are intended to avoid—it is critical that fluoride intake from dietary and nondietary sources be monitored in young children. To reduce the risk of dental fluorosis among formula-fed infants (89), the American Academy of Pediatrics (28) and the American Dental Association recommend using fluoride-free water or water with low fluoride levels for reconstituting infant formula. Since tap water is most commonly used for formula preparation (21), caregivers living in areas with fluoridated tap water may feel pressured to seek alternative water sources to minimize the risk of dental fluorosis. However, accessing low-fluoride water may be challenging and require additional financial resources or logistical efforts.

## 7.2. Risks Outweigh the Benefits

CWF is promoted as a simple and cost-effective strategy that reduces both caries prevalence across the population and socioeconomic disparities (115, 144). Every dollar invested in CWF has been estimated to save \$38 per person annually on dental treatment costs (22); this value does not consider the costs of operating and maintaining fluoridation equipment. CWF has been particularly endorsed for low-income communities lacking access to dental services (22). However, evidence that CWF reduces social inequalities in dental health is limited (77). A large-scale US study suggested that CWF attenuates income-related disparities in dental caries (120), whereas two recent studies in the United Kingdom (55, 98) and two Cochrane reviews (76, 77) did not.

An economic analysis of CWF must also account for the costs associated with any adverse effects, including effects on the developing brain. Using benchmark dose modeling, Grandjean et al. (58) found that a urinary fluoride concentration of about 0.3 mg/L in pregnant women is associated with a loss of one IQ point. The median urinary fluoride concentration of pregnant women living in a fluoridated community is about 0.62 mg/L (95, 132), which translates to an average loss of two IQ points (i.e., 0.62/0.3). A decrease of one to two IQ points may not be clinically significant for an individual child, but it can have a substantial population impact on the number of children with intellectual disability. To estimate the economic impact of a two-point decrease in IQ, we used existing models from Attina et al. (6) and Gaylord et al. (50), which value one IQ point at \$22,268 (USD) over a lifetime. Although determining an exact net worth is difficult, the economic impact of a two-point decrease in IQ over a lifetime is estimated at about \$44,536 ( $2 \times \$22,268$ ). Considering the millions of individuals consuming fluoridated water, either naturally or through fluoridation, this translates to a staggering economic cost in the trillions of

dollars in the United States alone. The economic burden of fluoride exposure appears to outweigh the gains afforded by CWF.

### 7.3. Strategies for Safe Use of Fluoride in Pregnancy and Children

There is a need to educate the public and health care professionals working with pregnant women and caregivers on the safe use of fluoride (**Supplemental Figure 3**). To safeguard the developing child, pregnant women and caregivers can take steps to minimize fluoride intake while maintaining the topical benefits of fluoride, for example, avoiding foods and beverages (e.g., black tea) with high fluoride when pregnant and supervising young children to minimize inadvertent swallowing of fluoride toothpaste. Reducing fluoride intake during pregnancy would not disadvantage the fetus because fluoride's benefits are minimal until teeth erupt (44). Specialized water filtration systems can be used to remove fluoride from tap water (the main source of fluoride); however, not everyone can afford a filtration system, perpetuating inequalities among low-income children who may experience additional stressors, such as lead, highway traffic, and poor nutrition.

Pregnancy is a time of increased susceptibility to periodontal disease and caries due to physiological disruptions and changes in behavior (7, 29). Prevention of oral health problems requires maintenance of good oral health, which can be achieved by regular brushing twice a day and flossing daily (68). Ingestion of fluoride is not required for caries prevention.

While some studies (148) suggest that discontinuing CWF contributes to dental health issues, the certainty of evidence is low (77). Removal of fluoride from the water supply requires consideration of the need for oral disease prevention and health promotion strategies, particularly targeting high-risk groups, such as people in lower-SES strata for whom prevalence of dental caries is highest (107). Examples of such strategies include school-based programs that promote the safe use of topical fluorides, apply dental sealants, provide oral health education, and encourage the adoption of healthy dietary choices to reduce caries risk (81). Globally, toothpaste is the most widely used topical vehicle for fluoride (80), and supervised tooth brushing has shown particular efficacy in areas with elevated caries risk (27, 31). Reducing disparities in oral health between SES strata necessitates a complex approach that considers social determinants of health and goes beyond the use of CWF.

## 8. CONCLUSION

CWF played a significant role in reducing dental caries and improving oral health when it was first introduced over 75 years ago. However, as time passed, the landscape of dentistry and public health has evolved. Today, people use numerous fluoride-containing products, such as toothpaste, that offer targeted and highly effective protection against dental caries without the need to ingest fluoride.

While some countries continue to endorse community-wide fluoridation, its risk and benefits have come under scrutiny in recent years, driven by a growing body of evidence. The benefits of systemic fluorides must be counterbalanced against the potential for adverse health impacts, particularly in vulnerable populations. Given that fluoride offers minimal benefit to the fetus and infant, health organizations and regulatory bodies should urgently review their recommendations and regulations to ensure they protect the most vulnerable. Public health policies have a profound effect on the health of the population and must be based on prudent judgement of current scientific evidence. These policies must also focus on providing a framework that addresses oral health inequalities by improving affordability and access to basic dental care and prevention of caries.

## SUMMARY POINTS

1. The prevalence of dental caries has declined over the past few decades in affluent countries, but it remains a major health problem for children and adults.
2. Fluoride's mechanism of action in preventing dental caries is primarily topical and occurs after tooth eruption.
3. Fluoride-containing toothpaste and fluoridated drinking water are important sources of fluoride intake in young children.
4. Breast milk contains extremely low concentrations of fluoride, whereas infant formula reconstituted with fluoridated water can contribute to overexposure to fluoride and cause dental fluorosis.
5. Systemic fluoride exposure is associated with detrimental effects on bone strength, thyroid function, and cognitive development.
6. Given that fluoride offers little benefit to the fetus and young infant, community-wide administration of systemic fluoride may pose an unfavorable risk–benefit ratio for the pregnant woman, fetus, and infant.
7. Healthcare professionals and the public require clear guidelines on the amount of fluoride that is safe for ingestion, especially during sensitive periods of development.
8. Restricting sugar consumption can significantly reduce the risk of caries.

## FUTURE ISSUES

1. Groundwater and well water can have naturally high levels of fluoride, with approximately 180 million people currently at risk of exposure to fluoride in drinking water at concentrations  $>1.5$  mg/L (114). Global increases in temperature can contribute to increased aridity, particularly in many areas in Africa and Asia, resulting in increased water consumption needs and greater reliance on groundwater. With increased aridity and associated increases in pH, high concentrations of fluoride in water may result, placing more people at risk of health effects resulting from long-term ingestion of fluoride. It is critical to monitor naturally occurring fluoride content in drinking water.
2. High-quality studies in large populations are needed to confirm the shape of the dose–response relationship for fluoride and cognitive development. Sensitive populations, including pregnant women, formula-fed infants, and people with iodine deficiency or kidney dysfunction, should be studied in greater detail, and fluoride exposures from all sources should be assessed at the individual level.
3. Untreated dental caries is a global public health problem. Efforts to develop safe and effective strategies to prevent this common disease are critical, particularly among lower-to-middle-income countries where dental caries are increasing and health systems and oral health resources to address this burden are often inadequate.

## DISCLOSURE STATEMENT

C.T. served as a consultant for the Health Research Board, Dublin, Ireland, for which she received an honorarium. She has also received travel support and honoraria for lectures related to fluoride

neurotoxicity. H.H., B.L., and P.G. served as expert witnesses in California for the plaintiffs in a federal trial on fluoridation against the US Environmental Protection Agency (Food & Water Watch et al. v. United States Environmental Protection Agency et al., United States District Court for the Northern District of California). B.L. served as a nonretained expert witness in this federal case to describe the results of the fluoride studies using the MIREC cohort. He received no payment for his service. H.H. served as a nonretained expert witness in this federal case to describe the results of the fluoride studies using the ELEMENT cohort. He received reimbursement from the US Department of Justice for expenses for this service. P.G. served as an expert on fluoride for the International Program on Chemical Safety and also as an expert witness in the same federal case to review the general causation aspects of human fluoride exposure. E.A.M.-M. served as a consultant for the US Environmental Protection Agency, chairing a panel of experts that reviewed evidence to assess environmental exposure to fluoride and the relative source contribution (RSC) for water. The RSC was used to derive the Maximum Contaminant Level Goal, which was used to recommend a reduction in the optimal concentration for CWF. She also served as a consultant for the U.S. Centers for Disease Control and Prevention to assess the potential use of biomarkers of fluoride exposure in surveillance and the assessment of the potential use of dental fluorosis to monitor fluoride exposure, diagnosed via imaging techniques. She is also a member of the Caries Advisory Board for the Colgate-Palmolive Company. All authors hold federal research awards related to fluoride research. The authors are not aware of any other affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

## ACKNOWLEDGMENTS

This work was supported by National Institute of Environmental Health Science grant R01ES030365 and National Institutes of Health grant R01ES021446. The authors thank Jana El-Sabbagh for her assistance.

## LITERATURE CITED

1. Adkins EA, Brunst KJ. 2021. Impacts of fluoride neurotoxicity and mitochondrial dysfunction on cognition and mental health: a literature review. *Int. J. Environ. Res. Public Health* 18:12884
2. Agalakova NI, Nadei OV. 2020. Inorganic fluoride and functions of brain. *Crit. Rev. Toxicol.* 50(1):28–46
3. Amaechi BT, AbdulAzees PA, Alshareif DO, Shehata MA, Lima PP de CS, et al. 2019. Comparative efficacy of a hydroxyapatite and a fluoride toothpaste for prevention and remineralization of dental caries in children. *BDJ Open* 5:18
4. Arora S, Kumar JV, Moss ME. 2018. Does water fluoridation affect the prevalence of enamel fluorosis differently among racial and ethnic groups? *J. Public Health Dent.* 78(2):95–99
5. Arun AK, Rustveld L, Sunny A. 2022. Association between water fluoride levels and low birth weight: National Health and Nutrition Examination Survey (NHANES) 2013–2016. *Int. J. Environ. Res. Public Health* 19(15):8956
6. Attina TM, Hauser R, Sathyanarayana S, Hunt PA, Bourguignon J-P, et al. 2016. Exposure to endocrine-disrupting chemicals in the USA: a population-based disease burden and cost analysis. *Lancet Diabetes Endocrinol.* 4(12):996–1003
7. Azofeifa A, Yeung LF, Alverson CJ, Beltrán-Aguilar E. 2016. Dental caries and periodontal disease among U.S. pregnant women and nonpregnant women of reproductive age, National Health and Nutrition Examination Survey, 1999–2004. *J. Public Health Dent.* 76(4):320–29
8. Barbier O, Arreola-Mendoza L, Del Razo LM. 2010. Molecular mechanisms of fluoride toxicity. *Chem.-Biol. Interact.* 188(2):319–33
9. Bashash M, Marchand M, Hu H, Till C, Martinez-Mier EA, et al. 2018. Prenatal fluoride exposure and attention deficit hyperactivity disorder (ADHD) symptoms in children at 6–12 years of age in Mexico City. *Environ. Int.* 121:658–66

10. Beltrán-Aguilar ED, Barker L, Dye BA. 2010. Prevalence and severity of dental fluorosis in the United States, 1999–2004. Data Brief 53, Natl. Cent. Health Stat., Cent. Dis. Control Prev., Washington, DC
11. Broffitt B, Levy SM, Warren JJ, Cavanaugh JE. 2007. An investigation of bottled water use and caries in the mixed dentition. *J. Public Health Dent.* 67(3):151–58
12. Burt BA. 1999. The case for eliminating the use of dietary fluoride supplements for young children. *J. Public Health Dent.* 59(4):269–74
13. Buzalaf MAR. 2018. Review of fluoride intake and appropriateness of current guidelines. *Adv. Dent. Res.* 29(2):157–66
14. Buzalaf MAR, Granjeiro JM, Damante CA, de Ornelas F. 2001. Fluoride content of infant formulas prepared with deionized, bottled mineral and fluoridated drinking water. *ASDC J. Dent. Child.* 68(1):10–37
15. Buzalaf MAR, Pessan JP, Honorio HM, ten Cate JM. 2011. Mechanisms of action of fluoride for caries control. In *Fluoride and the Oral Environment*, Vol. 22, ed. M Buzalaf, pp. 97–114. Basel, Switz.: Karger
16. Buzalaf MAR, Whitford GM. 2011. Fluoride metabolism. *Monogr. Oral Sci.* 22:20–36
17. Cantoral A, Luna-Villa LC, Mantilla-Rodriguez AA, Mercado A, Lippert F, et al. 2019. Fluoride content in foods and beverages from Mexico City markets and supermarkets. *Food Nutr. Bull.* 40(4):514–31
18. Cantoral A, Téllez-Rojo MM, Malin AJ, Schnaas L, Osorio-Valencia E, et al. 2021. Dietary fluoride intake during pregnancy and neurodevelopment in toddlers: a prospective study in the progress cohort. *NeuroToxicology* 87:86–93
19. Castiblanco-Rubio GA, Martínez-Mier EA. 2022. Fluoride metabolism in pregnant women: a narrative review of the literature. *Metabolites* 12(4):324
20. CDC (Cent. Dis. Control Prev.). 2000. Achievements in public health, 1900–1999: fluoridation of drinking water to prevent dental caries. *JAMA* 283(10):1283–86
21. CDC (Cent. Dis. Control Prev.). 2023. Infant feeding. In *Results: breastfeeding and infant feeding practices*. Rep., CDC, Atlanta, GA. [https://www.cdc.gov/breastfeeding-data/studies/methods-results-ifps.html?CDC\\_AAref\\_Val=https://www.cdc.gov/breastfeeding/data/ifps/results.htm](https://www.cdc.gov/breastfeeding-data/studies/methods-results-ifps.html?CDC_AAref_Val=https://www.cdc.gov/breastfeeding/data/ifps/results.htm)
22. CDC (Cent. Dis. Control Prev.). 2023. About community water fluoridation. *CDC*. <https://www.cdc.gov/fluoridation/about/>
23. Cerklewski F. 1997. Fluoride bioavailability—nutritional and clinical aspects. *Nutr. Res.* 17(5):907–29
24. Chen L, Jia P, Liu Y, Wang R, Yin Z, et al. 2023. Fluoride exposure disrupts the cytoskeletal arrangement and ATP synthesis of HT-22 cell by activating the RhoA/ROCK signaling pathway. *Ecotoxicol. Environ. Saf.* 254:114718
25. Chan L, Mehra A, Saikat S, Lynch P. 2013. Human exposure assessment of fluoride from tea (*Camellia sinensis* L.): a UK based issue? *Food Res. Int.* 51(2):564–70
26. Choi AL, Sun G, Zhang Y, Grandjean P. 2012. Developmental fluoride neurotoxicity: a systematic review and meta-analysis. *Environ. Health Perspect.* 120(10):1362–68
27. Clark E, Foster Page LA, Larkins K, Leon de la Barra S, Murray Thomson W. 2019. Caries-preventive efficacy of a supervised school toothbrushing programme in Northland, New Zealand. *Community Dent. Health* 36(1):9–16
28. Clark MB, Keels MA, Slayton RL, Sect. Oral Health. 2020. Fluoride use in caries prevention in the primary care setting. *Pediatrics* 146(6):e2020034637
29. Corbella S, Taschieri S, Del Fabbro M, Francetti L, Weinstein R, Ferrazzi E. 2016. Adverse pregnancy outcomes and periodontitis: a systematic review and meta-analysis exploring potential association. *Quintessence Int.* 47(3):193–204
30. Cui Y, Zhang B, Ma J, Wang Y, Zhao L, et al. 2018. Dopamine receptor D2 gene polymorphism, urine fluoride, and intelligence impairment of children in China: A school-based cross-sectional study. *Ecotoxicol. Environ. Saf.* 165:270–77
31. Damle SG, Patil A, Jain S, Damle D, Chopal N. 2014. Effectiveness of supervised toothbrushing and oral health education in improving oral hygiene status and practices of urban and rural school children: a comparative study. *J. Int. Soc. Prev. Community Dent.* 4(3):175–81
32. Day TK, Powell-Jackson PR. 1972. Fluoride, water hardness, and endemic goitre. *Lancet* 299(7761):1135–38



33. Dean HT, Dixon RM, Cohen C. 1935. Mottled enamel in Texas. *Public Health Rep.* 50(13):424–42
34. Dec K, Łukomska A, Skonieczna-Żydecka K, Kolasa-Wołoskiuk A, Tarnowski M, et al. 2019. Long-term exposure to fluoride as a factor promoting changes in the expression and activity of cyclooxygenases (COX1 and COX2) in various rat brain structures. *Neurotoxicology* 74:81–90
35. DenBesten P, Li W. 2011. Chronic fluoride toxicity: dental fluorosis. *Monogr. Oral. Sci.* 22:81–96
36. Dong H, Yang X, Zhang S, Wang X, Guo C, et al. 2021. Associations of low level of fluoride exposure with dental fluorosis among U.S. children and adolescents, NHANES 2015–2016. *Ecotoxicol. Environ. Saf.* 221:112439
37. Duan Q, Jiao J, Chen X, Wang X. 2018. Association between water fluoride and the level of children's intelligence: a dose-response meta-analysis. *Public Health* 154:87–97
38. Dye BA, Barker LK, Selwitz RH, Lewis BG, Wu T, et al. 2007. Overview and quality assurance for the National Health and Nutrition Examination Survey (NHANES) oral health component, 1999–2002. *Community Dent. Oral. Epidemiol.* 35(2):140–51
39. EFSA Panel Contam. Food Chain. 2010. Scientific opinion on lead in food. *EFSA J.* 8(4):1570–70
40. Ekstrand J, Boreus LO, de Chateau P. 1981. No evidence of transfer of fluoride from plasma to breast milk. *Br. Med. J. (Clin. Res. Ed.)* 283(6294):761–62
41. Ekstrand J, Ziegler EE, Nelson SE, Fomon SJ. 1994. Fluoride pharmacokinetics in infancy. *Pediatr. Res.* 35(2):157–63
42. Esala S, Vuori E, Helle A. 1982. Effect of maternal fluorine intake on breast milk fluorine content. *Br. J. Nutr.* 48(2):201–4
43. Evans RW, Darvell BW. 1995. Refining the estimate of the critical period for susceptibility to enamel fluorosis in human maxillary central incisors. *J. Public Health Dent.* 55(4):238–49
44. Featherstone JDB. 1999. Prevention and reversal of dental caries: role of low level fluoride. *Community Dent. Oral. Epidemiol.* 27(1):31–40
45. Featherstone JDB. 2000. The science and practice of caries prevention. *J. Am. Dent. Assoc.* 131(7):887–99
46. Fejerskov O, Thylstrup A, Larsen MJ. 1981. Rational use of fluorides in caries prevention: a concept based on possible cariostatic mechanisms. *Acta Odontol. Scand.* 39(4):241–49
47. Ferreira MKM, Aragão WAB, Bittencourt LO, Puty B, Dionizio A, et al. 2021. Fluoride exposure during pregnancy and lactation triggers oxidative stress and molecular changes in hippocampus of offspring rats. *Ecotoxicol. Environ. Saf.* 208:111437
48. Fiore G, Veneri F, Di Lorenzo R, Generali L, Vinceti M, Filippini T. 2023. Fluoride exposure and ADHD: a systematic review of epidemiological studies. *Medicina* 59(4):797
49. Forestier F, Daffos F, Said R, Brunet CM, Guillaume PN. 1990. The passage of fluoride across the placenta. An intra-uterine study. *J. Gynecol. Obstet. Biol. Reprod.* 19(2):171–75
50. Gaylord A, Osborne G, Ghassabian A, Malits J, Attina T, Trasande L. 2020. Trends in neurodevelopmental disability burden due to early life chemical exposure in the USA from 2001 to 2016: a population-based disease burden and cost analysis. *Mol. Cell Endocrinol.* 502:110666
51. Goin DE, Padula AM, Woodruff TJ, Sherris A, Charbonneau K, Morello-Frosch R. 2024. Water fluoridation and birth outcomes in California. *Environ. Health Perspect.* 132(5):057004
52. Goodman C, Hall M, Green R, Hornung R, Martinez-Mier EA, et al. 2022. Maternal fluoride exposure, fertility and birth outcomes: the MIREC cohort. *Environ. Adv.* 7:100135
53. Goodman CV, Bashash M, Green R, Song P, Peterson KE, et al. 2022. Domain-specific effects of prenatal fluoride exposure on child IQ at 4, 5, and 6–12 years in the ELEMENT cohort. *Environ. Res.* 211:112993
54. Goodman CV, Hall M, Green R, Chevrier J, Ayotte P, et al. 2022. Iodine status modifies the association between fluoride exposure in pregnancy and preschool boys' intelligence. *Nutrients* 14(14):2920
55. Goodwin M, Walsh T, Whittaker W, Emsley R, Kelly MP, et al. 2024. The CATFISH study: an evaluation of a water fluoridation program in Cumbria, UK. *Community Dent. Oral. Epidemiol.* 52(4):590–600
56. Gopu BP, Azevedo LB, Duckworth RM, Subramanian MKP, John S, Zohoori FV. 2022. The relationship between fluoride exposure and cognitive outcomes from gestation to adulthood—a systematic review. *Int. J. Environ. Res. Public Health* 20(1):22

57. Grandjean P. 2019. Developmental fluoride neurotoxicity: an updated review. *Environ. Health* 18(1):110
58. Grandjean P, Meddis A, Nielsen F, Beck IH, Bilenberg N, et al. 2023. Dose dependence of prenatal fluoride exposure associations with cognitive performance at school age in three prospective studies. *Eur. J. Public Health* 34(1):143–49
59. Green R, Lanphear B, Hornung R, Flora D, Martinez-Mier EA, et al. 2019. Association between maternal fluoride exposure during pregnancy and IQ scores in offspring in Canada. *JAMA Pediatr.* 173(10):940–48
60. Green R, Rubenstein J, Popoli R, Capulong R, Till C. 2020. Sex-specific neurotoxic effects of early-life exposure to fluoride: a review of the epidemiologic and animal literature. *Curr. Epidemiol. Rep.* 7(4):263–73
61. Griffin SO, Regnier E, Griffin PM, Huntley V. 2007. Effectiveness of fluoride in preventing caries in adults. *J. Dent. Res.* 86(5):410–15
62. Groeneveld A, Van Eck AA, Kalsbeek H, Theuns HM. 1988. De gebitstoestand van 15-jarigen: resultaten van een jaarlijks onderzoek in Tiel en Culemborg. [Dental caries in 15-year-old children in Tiel and Culemborg]. *Ned. Tijdschr. Tandheelkd.* 95(8):307–11 (In Dutch)
63. Gupta S, Seth AK, Gupta A, Gavane AG. 1993. Transplacental passage of fluorides. *J. Pediatr.* 123(1):139–41
64. Hall M, Hornung R, Chevrier J, Ayotte P, Lanphear B, Till C. 2024. Fluoride exposure and thyroid hormone levels in pregnancy: the MIREC cohort. *Environ. Int.* 184:108442
65. Hall M, Lanphear B, Chevrier J, Hornung R, Green R, et al. 2023. Fluoride exposure and hypothyroidism in a Canadian pregnancy cohort. *Sci. Total Environ.* 869:161149
66. Hall M, Lanphear B, Chevrier J, Hornung R, Green R, et al. 2024. Letter to the editor regarding Hall et al. (2023): fluoride exposure and hypothyroidism in a Canadian pregnancy cohort. *Sci. Total Environ.* 933:173121
67. Harriehausen CX, Dosani FZ, Chiquet BT, Barratt MS, Quock RL. 2019. Fluoride intake of infants from formula. *J. Clin. Pediatr. Dent.* 43(1):34–41
68. Hartnett E, Haber J, Krainovich-Miller B, Bella A, Vasilyeva A, Lange Kessler J. 2016. Oral health in pregnancy. *J. Obstet. Gynecol. Neonatal. Nurs.* 45(4):565–73
69. He H, Cheng Z, Liu W. 2008. Effects of fluorine on the human fetus. *Fluoride* 41(4):321–26
70. Heller KE, Sohn W, Burt BA, Feigal RJ. 2000. Water consumption and nursing characteristics of infants by race and ethnicity. *J. Public Health Dent.* 60(3):140–46
71. Helte E, Vargas CD, Kippler M, Wolk A, Michaëlsson K, Åkesson A. 2021. Fluoride in drinking water, diet, and urine in relation to bone mineral density and fracture incidence in postmenopausal women. *Environ. Health Perspect.* 129(4):047005
72. Hong L, Levy SM, Broffitt B, Warren JJ, Kanellis MJ, et al. 2006. Timing of fluoride intake in relation to development of fluorosis on maxillary central incisors. *Community Dent. Oral Epidemiol.* 34(4):299–309
73. Hung M, Hon ES, Mohajeri A, Moparthi H, Vu T, et al. 2023. A national study exploring the association between fluoride levels and dental fluorosis. *JAMA Netw. Open.* 6(6):e2318406
74. Iamandii I, De Pasquale L, Giannone ME, Veneri F, Generali L, et al. 2024. Does fluoride exposure affect thyroid function? A systematic review and dose-response meta-analysis. *Environ. Res.* 242:117759
75. Ibarluzea J, Gallastegi M, Santa-Marina L, Jiménez Zabala A, Arranz E, et al. 2022. Prenatal exposure to fluoride and neuropsychological development in early childhood: 1-to 4 years old children. *Environ. Res.* 207:112181
76. Iheozor-Ejiofor Z, Worthington HV, Walsh T, O'Malley L, Clarkson JE, et al. 2015. Water fluoridation for the prevention of dental caries. *Cochrane Database Syst. Rev.* 10:CD010856.pub2
77. Iheozor-Ejiofor Z, Walsh T, Lewis SR, Riley P, Boyers D, et al. 2024. Water fluoridation for the prevention of dental caries. *Cochrane Database Syst. Rev.* 10:CD010856.pub3
78. Inst. Med. 2006. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements.* Washington, DC: Natl. Acad. Press
79. Johnston NR, Strobel SA. 2020. Principles of fluoride toxicity and the cellular response: a review. *Arch. Toxicol.* 94(4):1051–69
80. Jones S, Burt BA, Petersen PE, Lennon MA. 2005. The effective use of fluorides in public health. *Bull. World Health Organ.* 83(9):670–76

81. Jürgensen N, Petersen PE. 2013. Promoting oral health of children through schools—results from a WHO global survey 2012. *Community Dent. Health* 30(4):204–18
82. Kampouri M, Gustin K, Stråvik M, Barman M, Levi M, et al. 2022. Association of maternal urinary fluoride concentrations during pregnancy with size at birth and the potential mediation effect by maternal thyroid hormones: the Swedish NICE birth cohort. *Environ. Res.* 214:114129
83. Kampouri M, Zander E, Gustin K, Sandin A, Barman M, et al. 2024. Associations of gestational and childhood exposure to lead, cadmium, and fluoride with cognitive abilities, behavior, and social communication at 4 years of age: NICE birth cohort study. *Environ. Res.* 263:120123
84. Kearns CE, Glantz SA, Schmidt LA. 2015. Sugar industry influence on the scientific agenda of the National Institute of Dental Research's 1971 National Caries Program: a historical analysis of internal documents. *PLOS Med.* 12(3):e1001798
85. Krishnankutty N, Storgaard Jensen T, Kjær J, Jørgensen JS, Nielsen F, Grandjean P. 2022. Public-health risks from tea drinking: fluoride exposure. *Scand. J. Public Health* 50(3):355–61
86. Kumar S, Lata S, Yadav JP, Yadav JP. 2016. Relationship between water, urine and serum fluoride and fluorosis in school children of Jhajjar District, Haryana, India. *Appl. Water Sci.* 7(6):3377–84
87. Lanphear BP. 2015. The impact of toxins on the developing brain. *Annu. Rev. Public Health* 36:211–30
88. Leverett DH, Adair SM, Vaughan BW, Proskin HM, Moss ME. 1997. Randomized clinical trial of the effect of prenatal fluoride supplements in preventing dental caries. *Caries Res.* 31(3):174–79
89. Levy SM, Broffitt B, Marshall TA, Eichenberger-Gilmore JM, Warren JJ. 2010. Associations between fluorosis of permanent incisors and fluoride intake from infant formula, other dietary sources and dentifrice during early childhood. *J. Am. Dent. Assoc.* 141(10):1190–201
90. Levy SM, Guha-Chowdhury N. 1999. Total fluoride intake and implications for dietary fluoride supplementation. *J. Public Health Dent.* 59(4):211–23
91. Levy SM, Kohout FJ, Guha-Chowdhury N, Kiritsy MC, Heilman JR, Wefel JS. 1995. Infants' fluoride intake from drinking water alone, and from water added to formula, beverages, and food. *J. Dent. Res.* 74(7):1399–407
92. Lindsay SE, Smith S, Yang S, Yoo J. 2023. Community water fluoridation and rate of pediatric fractures. *JAAOS Glob. Res. Rev.* 7(10):e22.00221
93. Luke J. 2001. Fluoride deposition in the aged human pineal gland. *Caries Res.* 35(2):125–28
94. Malin AJ, Eckel SP, Hu H, Martínez-Mier EA, Hernandez-Castro I, et al. 2024. Maternal urinary fluoride and child neurobehavior at age 36 months. *JAMA Netw. Open.* 7(5):e2411987
95. Malin AJ, Hu H, Martínez-Mier EA, Eckel SP, Farzan SF, et al. 2023. Urinary fluoride levels and metal co-exposures among pregnant women in Los Angeles, California. *Environ. Health* 22(1):74
96. Martínez-Mier EA, Soto-Rojas AE. 2010. Differences in exposure and biological markers of fluoride among White and African American children. *J. Public Health Dent.* 70(3):234–40
97. Miranda GH, Paz Alvarenga M, Ferreira M, Puty B, Bittencourt L, et al. 2021. A systematic review and meta-analysis of the association between fluoride exposure and neurological disorders. *Sci. Rep.* 11(1):22659
98. Moore D, Nyakutsikwa B, Allen T, Lam E, Birch S, et al. 2024. How effective and cost-effective is water fluoridation for adults and adolescents? The LOTUS 10-year retrospective cohort study. *Community Dent. Oral. Epidemiol.* 54(4):413–23
99. Morreale de Escobar G, Obregon MJ, Escobar del Rey F. 2004. Role of thyroid hormone during early brain development. *Eur. J. Endocrinol.* 151(Suppl. 3):U25–37
100. Moss ME, Luo H, Rosinger AY, Jacobs MIM, Kaur R. 2022. High sugar intake from sugar-sweetened beverages is associated with prevalence of untreated decay in US adults: NHANES 2013–2016. *Community Dent. Oral. Epidemiol.* 50(6):579–88
101. Nagata ME, Delbem ACB, Kondo KY, de Castro LP, Hall KB, et al. 2016. Fluoride concentrations of milk, infant formulae, and soy-based products commercially available in Brazil. *J. Public Health Dent.* 76(2):129–35
102. Natl. Cent. Health Stat., Natl. Cent. Chronic Dis. Prev. Health Promot. 2019. *Data quality evaluation of the dental fluorosis clinical assessment data from the National Health and Nutrition Examination Survey, 1999–2004 and 2011–2016*. Vital Health Stat. 183, Ser. 2, Natl. Cent. Health Stat., Cent. Dis. Control Prev., Hyattsville, MD

103. Natl. Health Med. Res. Council. 2017. *Nutrient reference values for Australia and New Zealand including recommended dietary intakes*. Rep., Natl. Health Med. Res. Council., Canberra, Aust.
104. Natl. Res. Council. 2006. *Fluoride in Drinking Water: A Scientific Review of EPA's Standards*. Washington, DC: The National Academies Press
105. Natl. Toxicol. Program. 2024. NTP monograph on the state of the science concerning fluoride exposure and neurodevelopment and cognition: a systematic review. Rep., Natl. Toxicol. Program, US Dept. Health Hum. Serv., Research Triangle Park, NC. <http://doi.org/10.22427/NTP-MGRAPH-8>
106. Neurath C, Limeback H, Osmunson B, Connert M, Kanter V, Wells CR. 2019. Dental fluorosis trends in US oral health surveys: 1986 to 2012. *JDR Clin. Trans. Res.* 4(4):298–308
107. Northridge ME, Kumar A, Kaur R. 2020. Disparities in access to oral health care. *Annu. Rev. Public Health* 41:513–35
108. O'Hagan-Wong K, Enax J, Meyer F, Ganss B. 2022. The use of hydroxyapatite toothpaste to prevent dental caries. *Odontology* 110(2):223–30
109. O'Mullane DM, Baez RJ, Jones S, Lennon MA, Petersen PE, et al. 2016. Fluoride and oral health. *Community Dent. Health* 33(2):69–99
110. Opydo J, Borysewicz-Lewickaa M. 2007. Transplacental passage of fluoride in pregnant Polish women assessed on the basis of fluoride concentrations in maternal and cord blood plasma. *Fluoride* 40:46–50
111. Ortíz-García SG, Torres-Sánchez LE, Muñoz-Rocha TV, Mercado-García A, Peterson KE, et al. 2022. Maternal urinary fluoride during pregnancy and birth weight and length: results from ELEMENT cohort study. *Sci. Total Environ.* 838(Part 3):156459
112. Paszynska E, Pawinska M, Enax J, Meyer F, Schulze zur Wiesche E, et al. 2023. Caries-preventing effect of a hydroxyapatite-toothpaste in adults: a 18-month double-blinded randomized clinical trial. *Front. Public Health* 11:1199728
113. Petrović B, Kojić S, Milić L, Luzio A, Perić T, et al. 2023. Toothpaste ingestion-evaluating the problem and ensuring safety: systematic review and meta-analysis. *Front. Public Health* 11:1279915
114. Podgorski J, Berg M. 2022. Global analysis and prediction of fluoride in groundwater. *Nat. Commun.* 13(1):4232
115. Public Health Agency Can. 2022. *The state of community water fluoridation across Canada*. Rep., Public Health Agency Can., Ottawa, ON, Can. <https://www.canada.ca/en/public-health/services/publications/healthy-living/community-water-fluoridation-across-canada.html>
116. Rao GS. 1984. Dietary intake and bioavailability of fluoride. *Annu. Rev. Nutr.* 4:115–36
117. Riddell JK, Malin AJ, Flora D, McCague H, Till C. 2019. Association of water fluoride and urinary fluoride concentrations with attention deficit hyperactivity disorder in Canadian youth. *Environ. Int.* 133(Part B):105190
118. Riddell JK, Malin AJ, McCague H, Flora DB, Till C. 2021. Urinary fluoride levels among Canadians with and without community water fluoridation. *Int. J. Environ. Res. Public Health* 18(12):6203
119. Rugg-Gunn AJ, Villa AE, Buzalaf MAR. 2011. Contemporary biological markers of exposure to fluoride. *Fluoride Oral Environ.* 22:37–51
120. Sanders AE, Grider WB, Maas WR, Curiel JA, Slade GD. 2019. Association between water fluoridation and income-related dental caries of US children and adolescents. *JAMA Pediatr.* 173(3):288–90
121. Shimonovitz S, Patz D, Ever-Hadani P, Singer L, Zacad D, et al. 1995. Umbilical cord fluoride serum levels may not reflect fetal fluoride status. *J. Perinat. Med.* 23(4):279–82
122. Singer L, Ophaug R. 1979. Total fluoride intake of infants. *Pediatrics* 63(3):460–66
123. Singh KA, Spencer AJ. 2004. Relative effects of pre- and post-eruption water fluoride on caries experience by surface type of permanent first molars. *Community Dent. Oral. Epidemiol.* 32(6):435–46
124. Singh KA, Spencer AJ, Brennan DS. 2007. Effects of water fluoride exposure at crown completion and maturation on caries of permanent first molars. *Caries Res.* 41(1):34–42
125. Sohn W, Noh H, Burt BA. 2009. Fluoride ingestion is related to fluid consumption patterns. *J. Public Health Dent.* 69(4):267–75
126. Sudradjat H, Meyer F, Fandrich P, Schulze Zur Wiesche E, Limeback H, Enax J. 2024. Doses of fluoride toothpaste for children up to 24 months. *BDJ Open* 10(1):7
127. Taher MK, Momoli F, Go J, Hagiwara S, Ramoju S, et al. 2024. Systematic review of epidemiological and toxicological evidence on health effects of fluoride in drinking water. *Crit. Rev. Toxicol.* 54(1):2–34

128. Takahashi R, Ota E, Hoshi K, Naito T, Toyoshima Y, et al. 2017. Fluoride supplementation (with tablets, drops, lozenges or chewing gum) in pregnant women for preventing dental caries in the primary teeth of their children. *Cochrane Database Syst. Rev.* 2017(10):CD011850
129. Taylor KW, Eftim SE, Sibrizzi CA, Blain RB, Magnuson K, et al. 2024. Fluoride exposure and children's IQ scores: a systematic review and meta-analysis. *JAMA Pediatr.* <https://doi.org/10.1001/jamapediatrics.2024.5542>
130. Thornton-Evans G, Junger ML, Lin M, Wei L, Espinoza L, Beltran-Aguilar E. 2019. Use of toothpaste and toothbrushing patterns among children and adolescents—United States, 2013–2016. *Morb. Mortal. Wkly. Rep.* 68(4):87–90
131. Till C, Green R, Flora D, Hornung R, Martinez-Mier EA, et al. 2020. Fluoride exposure from infant formula and child IQ in a Canadian birth cohort. *Environ. Int.* 134:105315
132. Till C, Green R, Grundy JG, Hornung R, Neufeld R, et al. 2018. Community water fluoridation and urinary fluoride concentrations in a national sample of pregnant women in Canada. *Environ. Health Perspect.* 126(10):107001
133. Tylanda CA, Jones D. 2003. *Toxicological profile for fluorides, hydrogen fluoride, and fluorine (update)*. Rep., Agency Toxic Subst. Dis. Regist., Atlanta, Georgia
134. US EPA (Environ. Prot. Agency). 2010. Fluoride: exposure and relative source contribution analysis. Rep., Health Ecol. Criteria Div., Off. Water, EPA, Washington, DC. <https://www.epa.gov/sites/default/files/2019-03/documents/fluoride-exposure-relative-report.pdf>
135. US Dep. Health Hum. Serv. Fed. Panel Community Water Fluorid. 2015. U.S. Public Health Service recommendation for fluoride concentration in drinking water for the prevention of dental caries. *Public Health Rep.* 130(4):318–31
136. Uyghurturk DA, Goin DE, Martinez-Mier EA, Woodruff TJ, Denbesten PK. 2020. Maternal and fetal exposures to fluoride during mid-gestation among pregnant women in northern California. *Environ. Health* 19(1):38
137. Valdez Jiménez L, López Guzmán OD, Cervantes Flores M, Costilla-Salazar R, Calderón Hernández J, et al. 2017. In utero exposure to fluoride and cognitive development delay in infants. *NeuroToxicology* 59:65–70
138. Veneri F, Vinceti M, Generali L, Giannone ME, Mazzoleni E, et al. 2023. Fluoride exposure and cognitive neurodevelopment: systematic review and dose-response meta-analysis. *Environ. Res.* 221:115239
139. Walsh T, Worthington HV, Glenny A-M, Marinho VC, Jeronic A. 2019. Fluoride toothpastes of different concentrations for preventing dental caries. *Cochrane Database Syst. Rev.* 3(3):CD007868
140. Wang A, Duan L, Huang H, Ma J, Zhang Y, et al. 2022. Association between fluoride exposure and behavioural outcomes of school-age children: a pilot study in China. *Int. J. Environ. Health Res.* 32(1):232–41
141. Wang D, Cao L, Pan S, Wang G, Wang L, et al. 2021. Sirt3-mediated mitochondrial dysfunction is involved in fluoride-induced cognitive deficits. *Food Chem. Toxicol.* 158:112665
142. Warren JJ, Levy SM, Broffitt B, Cavanaugh JE, Kanellis MJ, Weber-Gasparoni K. 2009. Considerations on optimal fluoride intake using dental fluorosis and dental caries outcomes—a longitudinal study. *J. Public Health Dent.* 69(2):111–15
143. Waugh D, Potter W, Limeback H, Godfrey M. 2016. Risk assessment of fluoride intake from tea in the Republic of Ireland and its implications for public health and water fluoridation. *Int. J. Environ. Res. Public Health* 13(3):259
144. Whittaker W, Goodwin M, Bashir S, Sutton M, Emsley R, et al. 2024. Economic evaluation of a water fluoridation scheme in Cumbria, UK. *Community Dent. Oral. Epidemiol.* 52(4):601–12
145. WHO (World Health Org.). 2022. *Global oral health status report: towards universal health coverage for oral health by 2030*. Rep., WHO, Geneva. <https://www.who.int/team/noncommunicable-diseases/global-status-health-2022/>
146. Wiener RC, Shen C, Findley P, Tan X, Sambamoorthi U. 2018. Fluorosis over time : a comparison of National Health and Nutrition Examination Survey data from 2001–2002 and 2011–2012. *J. Dent. Hyg.* 92(1):23–29

147. Wong MCM, Clarkson J, Glenny AM, Lo ECM, Marinho VCC, et al. 2011. Cochrane Reviews on the benefits/risks of fluoride toothpastes. *J. Dent. Res.* 90(5):573–79
148. Yazdanbakhsh E, Bohlouli B, Patterson S, Amin M. 2024. Community water fluoride cessation and rate of caries-related pediatric dental treatments under general anesthesia in Alberta, Canada. *Can. J. Public Health* 115(2):305–14
149. Yu Y, Yang W, Dong Z, Wan C, Zhang J, et al. 2008. Neurotransmitters and receptor changes in the brains of fetuses from areas of endemic fluorosis. *Fluoride* 41(2):134–38
150. Zhang S, Zhang X, Liu H, Qu W, Guan Z, et al. 2015. Modifying effect of *COMT* gene polymorphism and a predictive role for proteomics analysis in children's intelligence in endemic fluorosis area in Tianjin, China. *Toxicol. Sci.* 144(2):238–45
151. Zhang X, Lu E, Stone SL, Diop H. 2019. Dental cleaning, community water fluoridation and preterm birth, Massachusetts: 2009–2016. *Matern. Child Health J.* 23(4):451–58
152. Zhao P, Yuan Q, Liang C, Ma Y, Zhu X, et al. 2024. GPX4 degradation contributes to fluoride-induced neuronal ferroptosis and cognitive impairment via mtROS-chaperone-mediated autophagy. *Sci. Total Environ.* 927:172069
153. Zohoori FV, Omid N, Sanderson RA, Valentine RA, Maguire A. 2018. Fluoride retention in infants living in fluoridated and non-fluoridated areas: effects of weaning. *Br. J. Nutr.* 121(1):74–81